UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/580,523	05/30/2000	Xiao-Mai Zhou	A7483	8284

23373 7590 06/19/2002

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, DC 20037

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/580,523	ZHOU, XIAO-MAI	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the corresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *4-9,11,12,14,15,17,18,20,21,23,24,26,27 and 29-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10,13,16,19,22,25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 1-3, 10, 13, 16, 19, 22, 25 and 28 are being examined.

The following are the remaining rejections.

This application contains claims 4-9, 11-12, 14-15, 17-18, 20-21, 23-24, 26-27, 29-69 drawn to an invention nonelected with traverse in Paper No.8. A complete reply to this final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 1-2, 10, 13, 16, 19, 22, 25 and 28 pertaining to lack of enablement for an isolated polypeptide, or a fragment thereof, which does not have a serine at a position corresponding to position 118 of SEQ ID NO:1, wherein said position is identified by "alignment" of said polypeptide, or a fragment thereof, to SEQ ID NO:1, remains for reasons already of record in paper No.9.

Applicant argues that means by which one could compare two sequences are disclosed on page 45 of the specification. Applicant further asserts that the claims are

amended to recite "at least 75% homology" and thus one would clearly be enable to practice the claimed invention.

Applicant's arguments set forth in paper No11 have been considered but are not deemed to be persuasive for the following reasons:

The specification at page 45 dicloses that the alignment of the amino acid sequences is performed using the sequence analysis software such as Lasergene biocomputing software, which allows identification of regions of sequence homology, such as the BH3 domain.

It is noted that the position 118 of SEQ ID NO:1 is within the BH3 domain.

The claims however encompass an isolated polypeptide or a fragment thereof, which does not have a serine at a position corresponding to position 118 a fragment thereof to SEQ ID NO:1, wherein said position is identified by any type of "alignment" of said polypeptide or a fragment thereof, to SEQ ID NO:1, without any point of reference.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE OF ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 1-2, 10, 13, 16, 19, 22, 25 and 28 pertaining to lack of enablement for an isolated polypeptide or a fragment thereof, which contains a domain at least 75% homologous to a BH3 domain of a naturally-occuring or wild type mammalian BAD, or which is "at least 75% homologous" to SEQ ID NO:1, remains for reasons already of record in paper No.9.

Appicant argues that one could easily determine the candidate protein having cell death promoting acitivty. Applicant further asserts that the claims have been amended

to recite "at least 75% homology" and thus one would easily be able to determine whether the candidate protein falls within the structural attributes of the claimed invention.

Applicant's arguments set forth in paper No:11 have been considered but are not deemed to be persuasive for the following reasons:

The specification discloses a single novel amino acid position, serine at position 155 which is in the BH3 domain of the murine BAD of SEQ ID NO:2, and which is critical for the phosphorylation of the murine BAD and promoting cell survival by preventing BAD heterodimer formation with Bcl-X_L, an apoptotic antagonist, wherein replacement of serine with alanine abolishes the phosphorylation of the murine BAD and consequently promoting cell death (Examples 1-2, on pages 72-77, and Example 9, on pages 87-93). The serine at position 118 of the human BAD of SEQ ID NO:1 correspond to the serine at position 115 of the murine BAD of SEQ ID NO:2 (p.7 and 40-41 and table 1 on page 42). The specification also discloses that besides the disclosed serine 155 in SEQ ID NO:2, two other serine positions 112 and 136 of the murine BAD of SEQ ID NO:2 are known in the art to be responsible for phosphorylation of SEQ ID NO:2 (specification page 4, first paragraph). The specification however does not disclose which other amino acid positions within SEQ ID NO:1 besides the above mentioned three serine positions are also responsible for the phosphorylation of SEQ ID NO:1, wherein mutation at those amino acid positions would promote cell death.

The claims 1-2, 10, 13, 16, 19, 22, 25 and 28 however read on a nucleotide sequence encoding variants of SEQ ID NO:1, wherein said variants have any type of

substitution, at any amino acid, throughout the length of the peptide, as well as insertions and deletions. In addition, the specification and all other pending claims do not place any limit on the number of amino acids that could be substituted, provided the difference between the claimed sequences and SEQ ID NO:1 is within 25%. No principle has been taught concerning correlating the amino acid position with the ability to phosphorylate and active the BAD sequence. Thus the scope of the claims includes numerous structural variants, wherein one could only perform the claimed invention by random experimentation. Further, one could not predict that there would exist another serine position besides the above mentioned three serine positions that would be responsible for the phosphophorylation of the BAD sequence, because not any amino acid in SEQ ID NO:1 is responsible for the phosphorylation and activation of SEQ ID NO:1.

In addition, the claims read on variants of SEQ ID NO:1, wherein any amino acids in the BH3 domain could be substituted, deleted or conjugated. As discussed in the previous Office action, even a single amino acid substitution wil often dramatically affect the biological activity and characteristics of a protein (Burgess et al, Lazar et al, Tao et al, and Gillies et al, all of record). Thus, it is unpredictable that the domain having at least 75% homology with BH3 domain, wherein any amino acids in the BH3 domain could be substituted, deleted or conjugated would function as claimed, such as being responsible for the formation of homodimers and heterodimers, both among and between Bcl-2 family members, as disclosed in the specification (p.3, lines 1-3).

In view of the above, it would be undue experimentation to practice the claimed invention.

REJECTION UNDER 35 USC 102

Rejection under 35 USC 102 (b) of claims 1-2, 10, 19, 22, 25 and 28 pertaining to anticipation by PN=5,965703, remains for reasons already of record in paper No.9.

It is noted that claim 3, drawn to a fragment of a polypeptide which is identical to SEQ ID NO:1, except that the amino acid at a position corresponding to position 118 of SEQ ID NO:1 is an amino acid other than serine, was inadvertently omitted in the rejection in the previous Office action. It is clear that similar to a fragment of claim 1, a fragment of claim 3 is the same as a fragment of the murine BAD sequence taught by '703 patent, which is 75% similar to the entire length of SEQ ID NO:1.

Applicant argues that the '703 patent does not disclose that the mouse BAD or the protein encoded by SEQ ID NO:3 has cell death promoting activities. While the cell death promoting activity is described for the human BAD, it is not confirmed for mouse BAD.

Applicant further argues that the function of murine BAD is largely mediated by one amino acid, serine 136. The absence of phosphorylation at this site leads to increased cell death. Thus a single amino acid change in BAD protein could abolish the activity of the protein. As shown in figure 2 of the 703' patent, there are a number of amino acid differences between human and murine BAD. Thus given only the amino

acid sequence of murine BAD one would not expect that it would also has cell death promoting activity, absent of some evidence demonstrating such activity.

Applicant's arguments set forth in paper No11 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the BH3 domain of the human BAD as shown in figure 3A in the specification is LRRMSDE, which is different only one amino acid from the sequence LRRMTDE of the mouse BAD, as shown in figure 2 of '703 patent. Thus the mouse BAD contains the domain LRRMTDE which is inherently at least 75% homologous to a BH3 domain of a naturally-occuring or wild type mammalian BAD.

Further, it is noted that cell death promoting activity is an inherent property of BAD, including mouse BAD, as the name indicates, ii.e a cell death regulator protein, and as shown by PN=5,622,852, the mouse BAD, which has exactly the same sequence as the mouse BAD disclosed in '703 (see the sequence in figure 2 in '703 and the sequence in figure 1 of '852) can accelerate apoptotic cell death induced by cytokine deprivation in an IL-3 dependent cell line and counters the death repressor activity of bcl-X^L (column 5, paragraph before last, column 54 and figure 11 in '852 patent).

Thus the sequence and fragments thereof taught by the art meet all the limitations of the claims. That is: a) it inherently contains a domain at least 75% homologous to a BH3 domain of a naturally- occuring or wild type mammalian BAD, b) it does not have serine at position corresponding position 118 of SEQ ID NO:1 (as shown by the MPSRCH search report discussed in previous Office action), and c) it has cell

death promoting activity. Said sequence is at least 75% homologous to SEQ ID NO:1 (as shown by the MPSRCH search report discussed in previous Office action). Said sequence would bind to Bcl-X_L and Bcl-2 (colum 3, paragraph under detailed description of the invention, and column 6, second paragraph in '703 patent).

Further, although the reference does not specifically teach that the BAD sequence has cell death promoting activity, however, the claimed BAD sequence appears to be the same as the prior art BAD sequence. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

June 11, 2002

SUSAN UNGAR, PH.D
PRIMARY EXAMINER